REMARKS

Applicants have received and carefully reviewed the Office Action mailed January 3, 2005. Claims 1-40, 54-90, and 103-113 remain pending, with claims 69-80, 84, 88-90 and 108-109 withdrawn from consideration. As set forth above and further explained below, claims 1, 34, 54, 60 and 103 are amended herewith. Reconsideration, reexamination, and allowance of all pending claims are respectfully requested.

Applicants have amended claim 1 as follows:

> 1. A reference sample for maintaining prediction performance of an optical system used to measure an analyte or attribute in a representative measurement sample, wherein the representative measurement sample comprises a bodily tissue, bodily fluid or other biological sample containing the analyte or attribute and having a dominant absorbing species therein when in vivo, the reference sample comprising the dominant absorbing species *contained and disposed such that an optical signal interrogating the reference sample is subjected to diffuse reflection,* where the reference sample and the measurement sample absorb light at each of selected wavelengths in a manner to produce similarly shaped spectra over the wavelengths measured, wherein the measurement sample has the spectral characteristics of an in vivo sample.

Support for the underlined portion may be found at least, for example, in the Specification in the paragraph beginning on page 44, line 23. Support for the italicized portion may be found at least, for example, in the illustrative embodiments shown in Figures 5-20, which show various examples of the generic invention claimed.

Claim 34 has been amended as well:

> 34. A reference sample for maintaining prediction performance of an optical system used to measure an analyte or attribute in a representative measurement sample, the reference sample including a dominant absorbing species *housed in a structure defining a plurality of dispersive optical interfaces,* the dominant absorbing species corresponding to a dominant absorbing material present in the representative measurement sample when in vivo, wherein the representative measurement sample comprises a bodily tissue, bodily fluid or other biological sample containing the analyte or attribute, where the reference sample simulates the optical interaction between the measurement sample and the optical system.

Support for the underlined portion may be found at least, for example, in the Specification in the paragraph beginning on page 44, line 23. Support for the italicized portion may be found at

least, for example, in the illustrative embodiments shown in Figures 5-21, which show various examples of the generic invention claimed.

Claim 54 has been amended as follows:

> 54. A reference sample for maintaining prediction performance of an optical system used to measure an analyte or attribute in a representative measurement sample, wherein the representative measurement sample comprises a bodily tissue, bodily fluid or other biological sample containing the analyte or attribute as well as a dominant absorbing species present when the representative measurement sample is in vivo, where the reference sample has the same primary optical absorber as the measurement sample, wherein the measurement sample has the spectral characteristics of an in vivo sample, the dominant absorbing species being the primary optical absorber, the dominant absorbing species being contained in a housing allowing optical interrogation thereof.

Support for the underlined portion may be found at least, for example, in the Specification in the paragraph beginning on page 44, line 23.

Claim 60 has been amended as follows:

> 60. A reference sample for maintaining prediction performance of an optical system used to measure an analyte or attribute in a representative measurement sample, wherein the representative measurement sample comprises a bodily tissue, bodily fluid or other biological sample containing the analyte or attribute, with the reference sample producing a non-stepwise reference spectrum that is optically similar to the representative measurement sample, both the reference sample and the representative measurement sample having a primary optical absorber corresponding to a dominant in vivo optical absorber for the representative measurement sample, the dominant absorbing species being contained in a housing allowing optical interrogation thereof.

Support for the underlined portion may be found at least, for example, in the Specification in the paragraph beginning on page 44, line 23.

Claim 103 has been amended as follows:

> 103. A reference sample for maintaining prediction performance of an optical system used to measure an analyte or attribute in a test sample of interest, wherein the test sample comprises a bodily tissue, bodily fluid or other biological sample containing the analyte or attribute, with the reference sample producing a reference sample spectrum that is similar to the test sample spectrum, the reference sample including a transmissive optical interface and an optical sampling compartment, the optical sampling compartment containing water and a diffusely reflective or scattering media *and including structure such that an*

optical signal passing through the transmissive optical interface encounters reflective surfaces at various pathlengths from the optical interface.

Support for the italicized portion may be found at least, for example, in the illustrative embodiments shown in Figures 5-19, which show various examples of the generic invention claimed.

In paragraph 2 of the Office Action, independent claims 1, 34, 54, and 60, along with several dependent claims thereof, were rejected under 35 U.S.C. §112, second paragraph, as being indefinite. Each of these claims, as set forth above, has, in varying degrees of detail, been amended. It is believed that these amendments provide positively claimed structural limitations in addition to the recited optical responses/characteristics and overcome the stated rejections under §112, second paragraph.

In paragraph 4 of the Office Action, claims 1-33 and 54-59 were rejected under 35 U.S.C. §102(e) as being anticipated by Cohenford et al. (U.S. Patent No. 6,146,897). With the above amendments, independent claims 1 and 54 have been amended to recite, in relevant part (and in similar but not identical terms), that the reference sample includes a dominant absorbing species corresponding to a dominant absorbing material present in the representative measurement sample when in vivo. With most biological samples, water is the dominant absorbing material including cervical samples as set forth in Cohenford et al. Cohenford et al. teach, quite clearly, that drying is advantageous, if not necessary, for their system, for example, at column 9, lines 3-40. Not only is the recited invention of claims 1 and 54 not disclosed by Cohenford et al., but it is also clearly taught against. Therefore, claims 1-33 and 54-59 are believed to be patentable over Cohenford et al.

In paragraph 5 of the Office Action, claims 34-40, 60-65, 68, 69 and 81-83 were rejected under 35 U.S.C. §102(e) as being anticipated by Fellows (U.S. Patent No. 6,078,042). With the above amendments, independent claim 34 has been amended to recite that the reference sample includes a dominant absorbing species corresponding to a dominant absorbing material present in the representative measurement sample when in vivo. Claim 60 has been amended to recite that both the reference sample and the representative measurement sample have a primary optical absorber corresponding to a dominant in vivo optical absorber for the representative measurement sample. Fellows teaches a system wherein an optical filter 6 is used to provide

filtering representative of attenuation that would occur when optical signal encounters a sample, rather than using the dominant species as recited. As such, the recited invention of claims 34 and 60 is not disclosed or even suggested by Fellows. Therefore claims 34 and 60, along with respective dependent claims 35-40, 61-65, 68, 69 and 81-83, are believed to be patentable over Fellows.

In paragraph 6 of the Office Action, claims 1, 18, 34, 103-107, 110, 111, and 113 were rejected under 35 U.S.C. §102(e) as being anticipated by Hoogenraad et al. (U.S. Patent No. 6,230,045).

Hoogenraad et al. suggest a container having a "calibration" medium that may be, as noted by the Examiner, the Intralipid solution. The patient's breast is inserted into the container and partly immersed in the calibration medium. The calibration medium shares an average attenuation coefficient with the patient's tissue. The calibration medium is housed in a generally round container. Hoogenraad et al. focuses on the shortest light path (methods explained beginning on page 5, line 15) because Hoogenraad et al. discusses an imaging method that is not interested in constituent data (such as constituent concentrations) but instead in variations in density that likely indicate tumors. Light reflecting off of a surface of the structure is therefore undesirable. Further, Hoogenraad et al. do not appear to discuss light reflecting off of any of the interior walls of the container.

Claim 1 recites, in relevant part, that the reference sample is contained and disposed such that an optical signal interrogating the reference sample is subjected to diffuse reflection. Claim 34 recites, in relevant part, that the reference sample is housed in a structure defining a plurality of dispersive optical interfaces. Claim 103 recites, in relevant part, a structure such that optical signal passing through the transmissive optical interface encounters reflective surfaces at various pathlengths from the optical interface. Each of these highlighted recitations defines the claims such that the disposition of the reference sample and/or the structure containing the reference sample is not disclosed in Hoogenraad et al. Therefore, claims 1, 18, 34 and 103-107 are believed to be patentable over Hoogenraad et al.

With respect to claim 110, it appears that the Examiner is citing Hoogenraad et al. as providing support for rejection of several claims that recite a reference sample and/or a reference device. Claim 110 recites:

> 110. A reference device for use with an optical system to maintain prediction performance of the optical system for a constituent of a representative measurement sample, the reference device comprising:
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> a reference material having a first optical similarity to the representative measurement sample; and
>
> a structure for containing the reference material in a geometric configuration adapted to give the reference device a second optical similarity to the representative measurement sample;
>
> wherein the second optical similarity is greater than the first optical similarity.

It appears that the Examiner is suggesting that the generally round container used by Hoogenraad et al. meets the "structure" recited in claim 110. It is not clear to Applicants how this may be, as the generally round container of Hoogenraad et al. does not appear to serve any such function, nor does it appear to provide any second optical similarity (for example, pathlength as shown in the various examples shown in Figures 5-20 of Applicants' specification) as recited.

It is understood that the Hoogenraad et al. optical system includes a light source that is divided into several optical sources (14-21) for the container, and several detectors (38-45) are connected to the container such that there are, in effect, several detectors (22-29) on the container. As a result, multiple path lengths through the container are defined. However, the calibration step has light passing from a single source (one of 14-21) through the calibration medium to a single location (one of 22-29), this step being repeated for each source/detector pair. The container does not define multiple pathlengths for any single step of optical interrogation. When the patient's breast is immersed in the solution, however, the patient tissue (aside from light passing between adjacent source/detector pairs) will provide multiple pathlengths. As a result, the optical similarity from the reference material (in the claim, this would be the first optical similarity) in Hoogenraad et al. would exceed the optical similarity generated by the structure (the "second optical similarity"), as pathlength variation caused by the actual sampling of patient tissue is not accounted for or simulated.

Reexamination and reconsideration are respectfully requested. It is respectfully submitted that all pending claims are now in condition for allowance. Issuance of a Notice of Allowance in due course is requested. If a telephone conference might be of assistance, please contact the undersigned attorney at (612) 677-9050.

Respectfully submitted,

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By their Attorney,

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